### (19) World Intellectual Property Organization

International Bureau





## (43) International Publication Date 18 August 2005 (18.08.2005)

**PCT** 

# (10) International Publication Number WO 2005/075437 A1

(51) International Patent Classification<sup>7</sup>: C07D 237/04, 401/12, 403/12, A61K 31/50, 31/501, A61P 11/08

(21) International Application Number:

PCT/EP2005/050412

(22) International Filing Date: 1 February 2005 (01.02.2005)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 04002413.5

4 February 2004 (04.02.2004) EI

(71) Applicant (for all designated States except US): ALTANA PHARMA AG [DE/DE]; Byk-Gulden-Str. 2, 78467 Konstanz (DE).

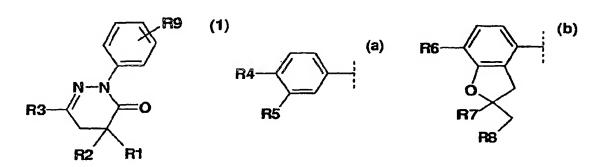
(72) Inventors (for AE, AG, AL, AM, AT, AU, AZ, BA, BB, BE, BG, BR, BW, BY, BZ, CH, CN, CO, CR, CU, CY, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FR, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, SZ, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW only): HATZELMANN, Armin; Alter Wall 3, 78467 Konstanz (DE). BARSIG, Johannes; Bleichenweg 11, 78467 Konstanz (DE). MARX,

Degenhard; Obere Reute 15, 78345 Moos (DE). KLEY, Hans-Peter; Im Weinberg 3b, 78476 Allensbach (DE). CHRISTIAANS, Johannes A. M.; Zevenwouden 233, NL-3524 CR UTRECHT (NL).

- (72) Inventors; and
- (75) Inventors/Applicants (for US only): MENGE, Wiro M. P. B. [NL/NL]; Pontanuslaan 11, NL-6821 HM ARNHEM (NL). STERK, Geert Jan [NL/NL]; Stadhouderslaan 38, NL-3583 JJ UTRECHT (NL).
- (74) Agents: WILD, Robert et al.; c/o ALTANA Pharma AG, 78467 Konstanz (DE).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,

[Continued on next page]

(54) Title: PYRIDAZINONE DERIVATIVES AND THEIR USE AS PDE4 INHIBITORS



(57) Abstract: Compounds of formula (1) are effective PDE4 inhibitors in which R1 is 1-4C-alkyl and R2 is 1-4C-alkyl, R3 represents a phenyl dervative of formulae (a) or (b) wherein R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R7 is 1-4C-alkyl and R8 is hydrogen or 1-4C-alkyl, or wherein R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom and R9 is hydroxyl, halogen, nitro, cyano, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxy which is completely or predominantly substituted by fluorine, hydroxycarbonyl, hydroxycarbonyl-1-4C-alkyl, 1-4C-alkoxycarbonyl, 1-4C-alkylcarbonyl, 1-4C-alkylcarbonyloxy, 1-4C-alkylsulfonyl, benzyloxy, -C(O)R10, -S(O)<sub>2</sub>-R11, -O(CH<sub>2</sub>)<sub>n</sub>-C(O)-R12, -(CH<sub>2</sub>), -C(O)-R26 or -N(R29)R30.



## WO 2005/075437 A1



FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### **Declarations under Rule 4.17:**

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,

NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

#### Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.